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Use of Opioid Analgesics in Pain Management



by **[Keith Candiotti, MD](#)**

Expert authors received compensation from Janssen Pharmaceuticals, Inc. for their contributions to [PrescribeResponsibly.com](#) History

Opioid analgesics have been used as medicinal agents, especially for the treatment of acute and chronic pain, for thousands of years. Ancient Greeks first identified and used these medicines, which were originally derived from opium — the latex of immature seed capsules of the poppy flower (*Papaver somniferum*).^{5,6} From these simple beginnings, opioid analgesics have become a mainstay of medical therapy used by millions of patients each year.⁷ While numerous drugs have been developed for the treatment of different types of pain, no single class of agent has replaced or reached the same level of usefulness for the treatment of moderate to severe pain as have opioid analgesics.⁸

Use of Opioid Analgesics in Pain Management

Opioid analgesics are often the first line of treatment for many painful conditions and may offer advantages over nonsteroidal anti-inflammatory drugs (NSAIDs). Opioid analgesics, for example, have no true "ceiling dose" for analgesia and do not cause direct organ damage; however, they do have several possible side effects, including constipation, nausea, vomiting, a decrease in sexual interest, drowsiness, and respiratory depression. With the exception of constipation, many patients often develop tolerance to most of the opioid analgesic-related side effects.⁸

While practitioners often express concern about the use of opioid analgesics for acute and chronic pain conditions, they are often the only suitable agent to control significant pain. This is especially true in the postoperative period.⁶⁰ Morphine is the most commonly used opioid analgesic in the postoperative period, but some practitioners prefer other agents, such as hydromorphone.⁹ There is some debate as to whether hydromorphone is better tolerated than morphine in terms of side

Another area of debate concerning opioid analgesics is their use in the treatment of neuropathic pain. This area is still being explored and remains somewhat controversial. Most studies related to this question have been small, demonstrated equivocal results, and have failed to clearly establish the long-term risk/benefit ratio of these agents.¹⁰ A recent Cochrane Review found that the results were somewhat mixed; short-term trials had contradictory results, while intermediate trials demonstrated opioid analgesic efficacy for spontaneous neuropathic pain. Across trials, the side effects were nausea, constipation, dizziness, and drowsiness.¹⁰

Mechanism of Action of Opioid Analgesics

Opioid analgesics bind to a number of different receptors throughout the body—mu, delta, and kappa.⁸ The binding to these different receptors results in both the therapeutic and adverse effects of opioid analgesics. Genetic variations in the structure of these receptors can partially explain interindividual responses, including some adverse reactions to these agents.¹¹

Adverse Reactions to Opioid Analgesics

Adverse reactions to opioid analgesics can be a limiting factor in the effective use of these drugs. In a study of patients taking opioid analgesics for prolonged periods of time, 80 percent of patients reported at least 1 adverse event, and 24 percent of patients discontinued therapy due to an adverse event.¹² Evaluation of the discontinuations due to adverse events demonstrated that constipation (41 percent), nausea (32 percent), vomiting (15 percent), and somnolence (29 percent) were the most common reasons cited for cessation of therapy.¹²

Early cessation or limitation of pain treatment due to adverse reactions can result in the inadequate treatment of pain. While more than just an inconvenience, the consequences of inadequate pain control can be far reaching and often are overlooked. Patients experiencing significant pain will have an increase in autonomic and sympathetic activity.³ Older patients, in particular, may develop delirium and cognitive dysfunction.¹³ The intensity of pain in the preoperative, intraoperative and early postoperative periods have been shown to be strong predictors for the development of chronic, persistent postoperative pain.¹⁴ While there are reports that excessive use of opioid analgesics may lead to a state of hyperalgesia,⁵ thus prompting some physicians to be concerned about using opioid analgesics for pain control, the lack of sufficient pain control may itself promote a hyperalgesic state in the form of persistent pain.³

Other Opioid Analgesic Concerns

Aside from medical issues related to opioid analgesics, there are nonmedical issues that may have an impact on prescribing patterns and patient use of these drugs. Practitioners are often concerned about prescribing opioid analgesics due to potential legal issues and questions of addiction.^{15,16} By the same token, patients report similar concerns about developing an addiction to opioid analgesics.¹⁷ While these concerns are not without some merit, it would appear that they are often overestimated. According to clinical opinion polls, true addiction occurs only in a small percentage of patients with chronic pain who receive chronic opioid analgesics analgesic therapy.¹⁸

Conclusion

To date, no agents have fully replaced opioid analgesics for the treatment of moderate to severe pain. While many patients and physicians have concerns about the use of opioid analgesics, which often prevent their use, it would appear that, with appropriate dosing and titration, they can be effective and safe medications for the treatment of painful conditions. In spite of how long these agents have been in clinical use, there still remains much to be learned, and ongoing research will no doubt help clarify some of these questions.

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This page was last modified on Jul 2 2015 at 10:02:50 EDT.